ture of equimolecular amounts (10 mg) of **5** and **19** was heated in a sealed tube under N_2 at 200° for 30 min. The lactone fraction was separated from unreacted starting material by tlc and analyzed by mass spectrometry. The mass spectrum showed four molecular ion peaks at *m/e* 167, 170, 181, and 184 (relative ratio: 47:47:4.7:1.3) indicating the presence of the four lactones presented in Scheme V.

Rearrangement of Methyl 1-Methyl-1-azabicyclo[2.2.2]oct-2-ene-3-carboxylate Perchlorate (1, X^- = ClO_4^-) in the Presence of Methyl 1-Azabicyclo[2.2.2]oct-2-ene-3-carboxylate (4). A mixture of 136 mg of 1 (X^- = ClO_4^-) and 81 mg of 4 was heated at 150° for 10 min. It was then treated with 3 ml of ether which after evaporation afforded 28 mg of **4**. Treatment of the crystalline residue with 5 ml of ethyl acetate, evaporation of the solvent, and recrystallization from ethyl acetate afforded 20 mg of **7**. Recrystallization of the residue from methanol yielded 85 mg of 1 (X^- = ClO_4^-). Under the above conditions, separate heating of 1 (X^- = ClO_4^-) and 4 afforded only unchanged starting material.

Registry No.—**1** iodide, 33402-77-6; **1** nitrate, 50790-74-4; **1** perchlorate, 50790-75-5; **1** hydrotosylate, 50790-76-6; **2** iodide, 33816-58-9; **3** iodide, 50790-77-7; **4**, 31539-88-5; **5**, 50790-78-8; **6**, 50790-79-9; **8**, 33689-31-5; **9**, 50790-80-2; **10**, 50790-81-3; **12**, 35593-77-2; **14**, 50790-82-4; **15**, 50790-83-5; **17**, 35645-77-3; **19**, 50790-84-6; 3-ethoxycarbonyl-3-hydroxyquinuclidine, 6238-31-9; 3-cyano-3-hydroxyquinuclidine, 6238-30-8; ethyl 1-azabicyclo[2.2.2]oct-2-ene-3-carboxylate HCl, 50790-85-7; ethyl 1-methyl-1-azabicyclo[2.2.2]oct-2-ene-3-carboxylate iodide, 50790-86-8; methyl 1-allyl-1-azabicyclo[2.2.2]oct-2-ene-3-carboxylate iodide, 50883-30-2; 3-cyano-3-hydroxy-6,8-dimethylquinuclidine, 50790-87-9; 6,8-dimethyl-3-quinuclidinone, 50790-88-0; 3-methoxycarbonyl-3-hydroxy-6,8-dimethylquinuclidine, 50790-89-1; azabicyclo[2.2.2]oct-2-ene-3-carboxylic acid HCl, 50790-90-4; 4-(2-hydroxyethyl)-1,4,5,6-tetrahydro-1-propynylnicotinic acid lactone, 50790-91-5; 1-allyl-4-(2-hydroxyethyl)-1,4,5,6-tetrahydronicotinic acid lactone, 50790-92-6.

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1-Imino-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole. Reactions with Electrophiles[1]

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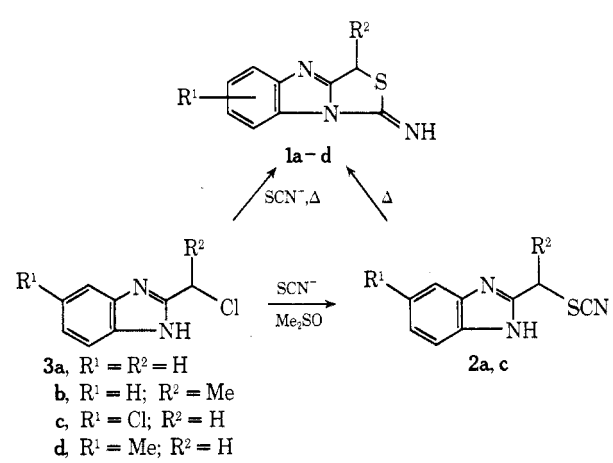
Intramolecular cyclization of 2-thiocyanoalkylbenzimidazole yielded the novel 1-imino-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole (**1**). Reaction of **1** with isocyanates gave exclusively the monoureas, **4**. Treatment of **1** with strong electrophiles (acid chlorides, tosyl chloride, and halocarbonates) furnished the derivatives **8**.

In a recent communication,[2] we reported a simple synthesis of the novel 1-imino-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole ring system (**1**) by the intermolecular cyclization of 2-thiocyanoalkylbenzimidazoles, **2** (Scheme I). Our interest in medicinal aspects of compounds derived from benzimidazole[3] prompted a study of the parent compound, **1a**.

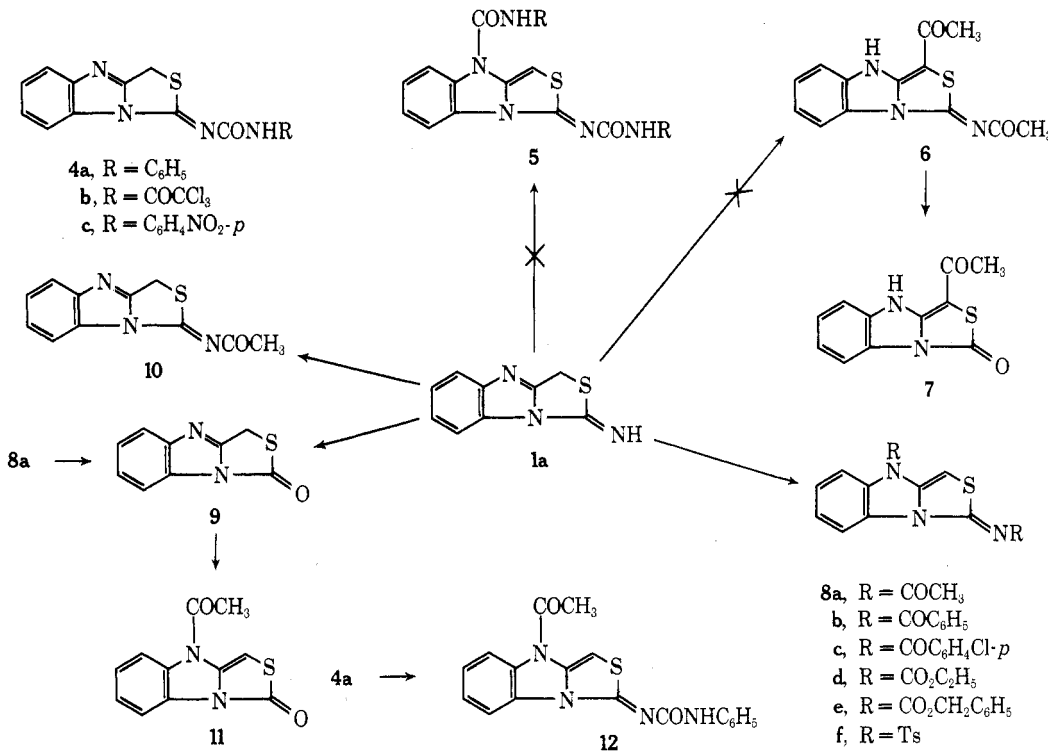
Initially, we sought solely to investigate reaction of the 1-imino group of **1a** with electrophiles. Treatment of **1a** with isocyanates yielded only the ureas, **4a–c**, rather than the enureas, **5**, that would be expected based on the results obtained by Chupp[4] with imines derived from cyclohexanone. Our efforts to synthesize the thioureas corresponding to **4** failed.

The product that resulted from heating of **1a** with acetic anhydride had an nmr spectrum that showed two methyl signals at δ 2.30 and 2.65 (DMSO-d_6) and a one-proton signal at δ 6.66 that was suggestive of a vinyl grouping. To distinguish between the two possible structures **6** and **8a**, we undertook the acid hydrolysis of this product. Whereas **6** should yield the enamino ketone **7**, hydrolysis of **8a** should furnish the cyclic thiocarbamate **9**. The nmr and ir data of the product obtained on the hydrolysis were identical with those of **9**, which was derived by acid treatment of **1a**, thus establishing the enamide structure **8a**. The postulated intermediate in this reaction, monoacetate **10**, was eventually isolated in 30% yield after we had acetylated **1a** with acetic anhydride for 3 min and quenched the reaction with water. However, even under these conditions, most of the starting material had already been converted to the diacetate **8a**. In analogous fashion we prepared enamides **8b** and **8c**, encarbamates **8d** and **8e**, and ensulfonamide **8f**. The product of hydrolysis of **1a**, namely **9** when acetylated with acetic anhydride gave the enamide **11**. Finally, monourea **4a**, when treated

Scheme I



Scheme II

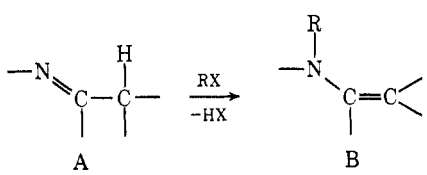


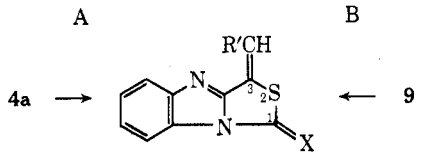
with acetic anhydride, yielded the urea enamide 12 (Scheme II). Similar "enacylamine" formations have been reported.[5-9]

It is suggested then that azomethines of type A, bearing a labile hydrogen (*i.e.*, enolizable imines), will, when exposed to very reactive electrophiles such as acid chlorides, acid anhydrides, tosyl chloride, and halocarbonates, yield substituted enamines, B. In the absence of the requisite α hydrogen, addition products or their displacement products[10] will be formed.

Lastly, derivatization of C_3 was achieved when **4a** or **9** was treated with the requisite aldehyde to furnish ylidenes **13a-d** (Scheme III).

Scheme III





13a, X = NCONHC$_6$H$_5$; R' = C$_6$H$_5$

b, X = NCONHC$_6$H$_5$; R' = 

c, X = NCONHC$_6$H$_5$; R' = 

d, X = O; R' = 

Experimental Section

Melting points were determined in capillary tubes on a Thomas-Hoover Uni-Melt apparatus and are uncorrected. Proton nmr spectra were obtained on a Varian A-60 instrument. Signals are described as singlet (s) or multiplet (m). For chromatography, neutral alumina (Woelm activity IV) was used.

2-Chloromethylbenzimidazoles (3). These derivatives were prepared according to known methods: **3a**,[11a] **3b**,[11b] **3c**,[11c] and **3d**.[11d]

Thiocyanic Acid (2-Benzimidazolyl)methyl Ester (2a). A solution of 8.4 g of ammonium thiocyanate and 9 g of 2-chloromethylbenzimidazole in 68 ml of dimethyl sulfoxide was stirred for about 15 min at room temperature. Water was added until no further precipitate formed, then the solid was filtered out and washed with water. Precipitation twice from dimethyl sulfoxide-water furnished, after drying, 4.2 g (41%) of the pure **2a**, mp 153-154°.

Anal. Calcd for $C_9H_7N_3S$: C, 57.20; H, 3.37; N, 22.23. Found: C, 57.10; H, 3.86; N, 21.96.

Thiocyanic Acid (5-Chloro-2-benzimidazolyl)methyl Ester (2c). A solution of 25 g of ammonium thiocyanate and 9.8 g of 5-chloro-2-chloromethylbenzimidazole in 125 ml of dimethyl sulfoxide was kept at 0° for 6 hr. Water was added, then the solid was filtered out and dried. Crystallization from chloroform-petroleum ether (bp 30-60°) yielded 4 g (38%) of **2c**, mp 125-128°.

Anal. Calcd for $C_9H_6ClN_3S$: C, 48.33; H, 2.70; N, 18.78. Found: C, 48.28; H, 2.98; N, 18.50.

1-Imino-1*H*-3*H*-thiazolo[3,4-*a*]benzimadazole (1a). Method A. A mixture of 1 g of 2-chloromethylbenzimidazole, 2 g of ammonium thiocyanate, and 30 ml of methanol was refluxed for 1 hr. The solvent was evaporated, then water was added to the residue and the solid was filtered off to yield 0.96 g (42%) of product, which was crystallized from methanol, mp 169-170°, mass spectrum *m/e* 189 (M^+).

Method B. A solution of 4.2 g of **2a** in 200 ml of methanol was refluxed for 1 hr. Water was added to the cooled solution until complete precipitation had been achieved. Recrystallization from methanol yielded 2 g (40%) of **1a**.

Anal. Calcd for $C_9H_7N_3S$: C, 57.12; H, 3.73; N, 22.20. Found: C, 57.23; H, 3.96; N, 22.20.

1-Imino-3-methyl-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole (1b). The preparation of **1b** was analogous to that of **1a**, method A (23%, after chromatography); **1b** had mp 117-118° (petroleum ether).

Anal. Calcd for $C_{10}H_9N_3S$: C, 59.09; H, 4.47; N, 20.67. Found: C, 59.25; H, 4.46; N, 20.46.

6- (and 7-) Chloro-1-imino-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole (1c). A mixture of 10 g of 2-chloromethyl-5-chlorobenzimidazole and 8 g of ammonium thiocyanate in 200 ml of dimethylformamide was heated for 3.5 hr at 50°. The mixture was allowed to stand overnight at room temperature. The solid that formed was filtered off and crystallized twice from ethyl ether to yield 6 g (59%) of pure **1c**, mp 156-158°.

Anal. Calcd for $C_9H_6ClN_3S$: C, 48.33; H, 2.70; N, 18.78. Found: C, 48.55; H, 2.96; N, 18.70.

Fractional crystallization from ether furnished two distinct crystal forms, bars and rosettes, which were separated by Pasteur's technique and recrystallized from ether. The rosettes had mp 158–159° (6 isomer); the bars had mp 161–162° (7 isomer).

6- (and 7-) Methyl-1-imino-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole (1d). The preparation of **1d** was analogous to that of **1c** (19%); **1d** had mp 152–153° (ether).

Anal. Calcd for $C_{10}H_9N_3S$: C, 59.10; H, 4.47; N, 20.67. Found: C, 59.08; H, 4.78; N, 20.48.

1-Phenyl-3-(1*H*,3*H*-thiazolo[3,4-*a*]benzimidazol-1-ylidene)-urea (4a). A mixture of 5.7 g of **1a**, 10 ml of phenyl isocyanate, and 50 ml of ethyl acetate was refluxed for 1 hr. The solvent was evaporated, and the resulting residue was crystallized twice from benzene to yield 4 g (43%) of **4a**, mp 160° (melts, solidifies, melts again at 195–197°).

1-(1*H*,3*H*-Thiazolo[3,4-*a*]benzimidazol-3-ylidene)-3-(trichloroacetyl)urea (4b). The preparation of **4b** was analogous to that of **4a** (33%); **4b** had mp 180–182° (DMSO-water).

1-(*p*-Nitrophenyl)-3-(1*H*,3*H*-thiazolo[3,4-*a*]benzimidazol-3-ylidene)urea (4c). The preparation of **4c** was analogous to that of **4a** (50%); **4c** had mp 260–262° (pyridine).

9-Acetyl-3-(acetylimino)-3*H*,9*H*-thiazolo[3,4-*a*]benzimidazole (8a). A mixture of 5 g of **1a**, 5 g of anhydrous sodium acetate, and 20 ml of acetic anhydride was heated on a steam bath for 0.25 hr. On cooling a solid separated, and was filtered off and washed with water. Crystallization from chloroform yielded 3 g (87%) of pure **8a**, mp 258–261°.

9-Benzoyl-3-(benzoylimino)-3*H*,9*H*-thiazolo[3,4-*a*]benzimidazole (8b). To a solution of 1.9 g of **1a** in 250 ml of ethyl acetate and 10 ml of pyridine, there was added 3.1 g of benzoyl chloride. The mixture was refluxed for 0.5 hr and was then filtered hot. The residue obtained after evaporation of the solvent was filtered, washed with water, and crystallized from ethyl acetate to furnish 2 g (50%) of **8b**, mp 232–234°.

9-(*p*-Chlorobenzoyl)-3(*p*-chlorobenzoylimino)-3*H*,9*H*-thiazolo[3,4-*a*]benzimidazole (8c). To a solution of 3.6 g of **1a** in 10 ml of triethylamine and 250 ml of ethyl acetate there was added, dropwise, 7 ml of *p*-chlorobenzoyl chloride. The mixture was then refluxed for 20 min. The resulting solid was filtered off, washed with water, and crystallized from pyridine to yield 6 g (65%) of **8c**, mp 220°.

1-(Carboxyimino)-1*H*,4*H*-thiazolo[3,4-*a*]benzimidazole-4-carboxylic Acid Diethyl Ester (8d). A mixture of 5 g of **1a** and 50 ml of freshly distilled chloroethyl carbonate was refluxed for 1.5 hr. The cooled mixture was filtered and the remaining solid was washed with 10% NaOH and water. The dried solid was crystallized once from ethyl acetate and then twice from benzene to furnish 1.2 g (27%) of **8d**, mp 162–163°.

1-(Carboxyimino)-1*H*,4*H*-thiazolo[3,4-*a*]benzimidazole-4-carboxylic Acid Dibenzyl Ester (8e). The preparation of **8e** was analogous to that of **8d** (25%); **8e** had mp 168–170°.

4-(*p*-Tolylsulfonyl)-1-[(*p*-tolylsulfonyl)imino]-1*H*,4*H*-thiazolo[3,4-*a*]benzimidazole (8f). A mixture of 3.78 g of **1a**, 8 g of *p*-toluenesulfonyl chloride, 8 ml of pyridine, and 300 ml of benzene was stirred at room temperature for 2 days. The benzene solution was decanted and evaporated. After treatment of the benzene residue with excess $NaHCO_3$ solution, the remaining solid was filtered off, then was crystallized twice from acetone to furnish 2 g (20%) of **8f**, mp 197–198°.

1*H*,3*H*-Thiazolo[3,4-*a*]benzimidazol-3-one (9). To 195 ml of hot, concentrated hydrochloric acid (90°) there was added 7.8 g of **1a**. The mixture was kept on a steam bath for 10 min. The solution was cooled and brought to pH 5 with concentrated ammonia. The resulting precipitate was filtered and crystallized twice from ethyl acetate to yield 2.8 g (38%) of **9**, mp 212–224°.

1-(Acetylimino)-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazole (10). A mixture of 0.5 g of **1a** and 20 ml of acetic anhydride was heated on a steam bath for about 1.5 min until the solid just dissolved. Water was added, and the resulting solid was filtered off, dried, and chromatographed on neutral Alumina (Woelm, activity IV). Elution with petroleum ether–ether (1:1) yielded the product, which was crystallized from petroleum ether–ether to yield 0.2 g (30%) of **10**, mp 195–197°.

4-Acetyl-1*H*,4*H*-thiazolo[3,4-*a*]benzimidazol-1-one (11). The preparation of **11** was analogous to that of **8a** (65%); **11** had mp 179–182° (ethyl acetate).

1-(4-Acetyl-1*H*,4*H*-thiazolo[3,4-*a*]benzimidazol-1-ylidene)-3-phenylurea (12). A mixture of 2.8 g of **4a** and 35 ml of acetic anhydride was heated on a steam bath for 15 min. The solid that formed was filtered out and crystallized from ethyl acetate to give 2.5 g (77%) of **12**, mp 153–155°.

1-(3-Benzylidene-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazol-1-ylidene)-3-phenylurea (13a). A mixture of 2.0 g of **8a** and 1.5 ml of benzaldehyde was refluxed for 3 min. After the reaction mixture had cooled, methanol was added. The resulting yellow solid was crystallized from chloroform–ether to yield 1.0 g (63%) of **13a**, mp 221–224°.

1-(3-Furfurylidene-1*H*,3*H*-thiazolo[1,2-*c*]benzimidazol-1-ylidene)-3-phenylurea (13b). The preparation of **13b** was analogous to that of **13a** (33%); **13b** had mp 230–234° (chloroform–ether).

1-Phenyl-3-[3-(2-thenylidene)-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazol-1-ylideneurea (13c). The preparation of **13c** was analogous to that of **13a** (42%); **13c** had mp 256–258° (ether).

3-Thenylidene-1*H*,3*H*-thiazolo[3,4-*a*]benzimidazol-1-one (13d). A solution of 2 g of **9** in 5 ml of 2-thiophenecarboxaldehyde was refluxed for 5 min. After the mixture had cooled, it was triturated with a few milliliters of methanol. The resulting yellow solid was filtered off and crystallized from chloroform to yield 1 g (35%) of **13d**, mp 211–212°.

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Registry No.—**1a**, 34580-85-3; **1b**, 34580-83-1; **1c** 6 isomer, 34580-81-9; **1c** 7 isomer, 34580-80-8; **1d** 6 isomer, 34580-79-5; **1d** 7 isomer, 34580-78-4; **2a**, 34091-38-8; **2c**, 34091-37-7; **4a**, 37506-42-6; **4b**, 37506-43-7; **4c**, 37601-96-0; **8a**, 37506-45-9; **8b**, 37506-46-0; **8c**, 51065-52-2; **8d**, 37506-48-2; **8e**, 51065-53-3; **8f**, 51065-54-4; **9**, 34580-84-2; **10**, 37506-44-8; **11**, 51065-55-5; **12**, 37506-47-1; **13a**, 51065-56-6; **13b**, 51065-57-7; **13c**, 51065-58-8; **13d**, 51065-59-9; 2-chloromethylbenzimidazole, 4857-04-9; 5-chloro-2-chloromethylbenzimidazole, 20443-38-3.

Supplementary Material Available. Analytical data for compounds **4a–c** and **8–13** and pertinent spectral data (ir and nmr) will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JOC-74-1359.

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